

## **AMENDMENTS TO THE CLAIMS:**

The listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of claims:**

1. (Withdrawn) A emulsion comprising: (a) an antidepressant or a pharmaceutically acceptable salt thereof; (b) an NMDA receptor antagonists or a pharmaceutically acceptable salt thereof; (c) a lipophilic component; (d) water; and (e) a surfactant, wherein the emulsion is an oil in water emulsion.
2. (Withdrawn) The emulsion of claim 1, wherein the mean oil droplet size is within the range of about 0.01 microns to about 100 microns.
3. (Withdrawn) The emulsion of claim 1, wherein the mean oil droplet size is within the range of about 0.1 microns to about 10 microns.
4. (Withdrawn) The emulsion of claim 1, wherein the antidepressant is a norepinephrine reuptake inhibitor, a selective serotonin reuptake inhibitor, a monoamine oxidase inhibitor, a serotonin and noradrenaline reuptake inhibitor, a corticotropin releasing factor antagonist, an  $\alpha$ . adrenoreceptor antagonist, an NK1 receptor antagonist, a 5 HT.sub.1A receptor agonist, a 5 HT.sub.1A receptor antagonist, a 5 HT.sub.1A receptor partial agonist, an atypical antidepressant, or an other antidepressant or a pharmaceutically acceptable salt thereof.
5. (Withdrawn) The emulsion of claim 4, wherein the antidepressant is a norepinephrin reuptake inhibitor or a pharmaceutically salt thereof.
6. (Withdrawn) The emulsion of claim 1, wherein the antidepressant is a tricyclic depressant or a pharmaceutically acceptable salt thereof.
7. (Withdrawn) The emulsion of claim 6, wherein the tricyclic antidepressant is amitriptyline, desmethyramitriptyline, clomipramine, doxepin, imipramine, imipramine N oxide, trimipramine; adinazolam, amitriptylinoxide, amoxapine, desipramine, maprotiline, nortriptyline, protriptyline, amineptine, butriptyline, demexiptiline, dibenzepin, dimetacrine,

dothiepin, fluacizine, iprindole, lofepramine, melitracen, metapramine, norclolipramine, noxiptilin, opipramol, perlapine, pizotyline, propizepine, quinupramine, reboxetine, or tianeptine or a pharmaceutically acceptable salt thereof.

8. (Withdrawn) The emulsion of claim 1, wherein the antidepressant is amitriptyline or a pharmaceutically acceptable salt thereof.

9. (Withdrawn) The emulsion of claim 1, wherein an amount of the antidepressant is within the range of about 0.1% by weight to about 10% by weight of a total weight of the emulsion.

10. (Withdrawn) The emulsion of claim 1, wherein the NMDA receptor antagonist is one that binds to the NMDA receptor at the glycine binding site, the glutamate binding site, the PCP binding site, the polyamine binding site, or the zinc binding site or a pharmaceutically acceptable salt thereof.

11. (Withdrawn) The emulsion of claim 10, wherein the NMDA receptor antagonist is one that binds to the NMDA receptor at the PCP binding site or a pharmaceutically acceptable salt thereof.

12. (Withdrawn) The emulsion of claim 1, wherein the NMDA receptor antagonist is ketamine, phencyclidine, dextromethorphan, dextrophan, dexoxadrol, dizocilpine, remacemide, thienylcyclohexylpiperidine, N-allylnormetazocine, cyclazocine, etoxadrol, (1,2,3,4,9,9a-hexahydro-fluoren-4a-yl)-methyl-amine, (1,3,4,9,10,10a-hexahydro-2H-phenanthren-4a-yl)-methyl-amine, PD 138558, tiletamine, kynurenic acid, 7-chloro-kynurenic acid, memantine, 6-cyano-7-nitroquinoxaline-2,3-dione, or 6,7-dinitroquinoxaline-2,3-dione or a pharmaceutically acceptable salt thereof.

13. (Withdrawn) The emulsion of claim 1, wherein the NMDA receptor antagonist is ketamine or a pharmaceutically acceptable salt thereof.

14. (Withdrawn) The emulsion of claim 1, wherein an amount of the NMDA receptor antagonist is within the range of about 0.1% by weight to about 10% by weight of a total weight of the emulsion.

15. (Withdrawn) The emulsion of claim 1, wherein the NMDA receptor antagonist is ketamine or a pharmaceutically acceptable salt thereof and the antidepressant is amitriptyline or a pharmaceutically acceptable salt thereof.

16. (Withdrawn) The emulsion of claim 1, wherein the lipophilic component comprises petrolatum.

17. (Withdrawn) The emulsion of claim 1, wherein the lipophilic component comprises a stiffening agent.

18. (Withdrawn) The emulsion of claim 17, wherein the stiffening agent is cetyl alcohol.

19. (Withdrawn) The emulsion of claim 1, further comprising a lipophilic intradermal penetration enhancer.

20. (Withdrawn) The emulsion of claim 19, wherein the lipophilic intradermal penetration enhancer is isopropyl myristate, glycerol monolaurate, glycerol monooleate, glycerol monolinoleate, isopropyl isostearate, isopropyl linoleate, isopropyl myristate/fatty acid monoglyceride combination, isopropyl myristate/ethanol/L-lactic acid combination, isopropyl palmitate, methyl acetate, methyl caprate, or methyl laurate.

21. (Withdrawn) The emulsion of claim 1 further comprising a humectant or an anti-foaming agent.

22. (Withdrawn) A patch comprising: (a) an antidepressant or a pharmaceutically acceptable salt thereof; (b) an NMDA receptor antagonists or a pharmaceutically acceptable salt thereof; (c) a lipophilic component; (d) water; and (e) a surfactant, wherein the emulsion is an oil in water emulsion.

23. (Withdrawn) The patch of claim 22, wherein the NMDA receptor antagonist is ketamine or a pharmaceutically acceptable salt thereof and the antidepressant is amitriptyline or a pharmaceutically acceptable salt thereof.

24. (Currently Amended) A method of treating pain in a mammal comprising topically administering to the skin of a mammal ~~in need thereof~~ an emulsion comprising:

- (a) a therapeutically effective amount of an antidepressant or a pharmaceutically acceptable salt thereof;
- (b) a therapeutically effective amount of ~~[[an]]~~ ~~[[NMDA]]~~ N-methyl-D-aspartate receptor antagonist[s] or a pharmaceutically acceptable salt thereof;
- (c) a lipophilic component;
- (d) water; ~~[[and]]~~
- (e) a surfactant, wherein the emulsion is an oil in water emulsion, and wherein the antidepressant is a norepinephrine reuptake inhibitor, a selective serotonin reuptake inhibitor, a monoamine oxidase inhibitor, a serotonin and noradrenaline reuptake inhibitor, a corticotropin releasing factor antagonist, an .alpha. adrenoreceptor antagonist, an neurokinin 1 receptor antagonist, a 5 hydroxytryptamine sub.1A receptor agonist, a 5 HT.sub.1A receptor antagonist, a 5 HT.sub.1A receptor partial agonist, an atypical antidepressant, or an other antidepressant or a pharmaceutically acceptable salt thereof.

25. (Previously Presented) The method of claim 24, wherein the emulsion has a mean oil droplet size within the range of about 0.01 microns to about 100 microns.

26. (Previously Presented ) The method of claim 24, wherein the emulsion has a mean oil droplet size within the range of about 0.1 microns to about 10 microns.

27. (Cancelled)

28. (Withdrawn)

29. (Previously Presented) The method of claim 24, wherein the antidepressant is a tricyclic depressant or a pharmaceutically acceptable salt thereof.

30. (Previously Presented) The method of claim 29, wherein the tricyclic antidepressant is amitriptyline, desmethyramitriptyline, clomipramine, doxepin, imipramine, imipramine N-oxide, trimipramine; adinazolam, amitriptylinoxide, amoxapine, desipramine, maprotiline, nortriptyline, protriptyline, amineptine, butriptyline, demexiptiline, dibenzepin,

dimetacrine, dothiepin, fluacizine, iprindole, lofepramine, melitracen, metapramine, norclolipramine, noxiptilin, opipramol, perlapine, pizotyline, propizepine, quinupramine, reboxetine, or tianeptine or a pharmaceutically acceptable salt thereof.

31. (Previously Presented) The method of claim 24, wherein the antidepressant is amitriptyline or a pharmaceutically acceptable salt thereof.

32. (Currently Amended) The method of claim 24, wherein [an] the therapeutically effective amount of the antidepressant is within the range of about 0.1% by weight to about 10% by weight of a total weight of the emulsion.

33. (Currently Amended) The method of claim 24, wherein the NMDA receptor antagonist is one that binds to the NMDA receptor at the glycine binding site, the glutamate binding site, the [[PCP]] phencyclidine binding site, the polyamine binding site, or the zinc binding site ~~or a pharmaceutically acceptable salt thereof~~.

34. (Currently Amended) The method of claim 33, wherein the NMDA receptor antagonist is one that binds to the NMDA receptor at the PCP binding site ~~or a pharmaceutically acceptable salt thereof~~.

35. (Previously Presented) The method of claim 24, wherein the NMDA receptor antagonist is ketamine, phencyclidine, dextromethorphan, dextrophan, dexoxadrol, dizocilpine, remacemide, thienylcyclohexylpiperidine, N-allylnormetazocine, cyclazocine, etoxadrol, (1,2,3,4,9,9a-hexahydro-fluoren-4a-yl)-methyl-amine, (1,3,4,9,10,10a-hexahydro-2H-phen- anthren-4a-yl)-methyl-amine, PD 138558, tiletamine, kynurenic acid, 7-chloro-kynurenic acid, memantine, 20 6-cyano-7-nitroquinoxaline-2,3-dione, or 6,7-dinitro-quinoxaline-2,3-dione or a pharmaceutically acceptable salt thereof.

36. (Previously Presented) The method of claim 24, wherein the NMDA receptor antagonist is ketamine or a pharmaceutically acceptable salt thereof.

37. (Currently Amended) The method of claim 24, wherein [an] the therapeutically effective amount of the NMDA receptor antagonist is within the range of about 0.1% by weight to about 10% by weight of a total weight of the emulsion.

38. (Previously Presented) The method of claim 24, wherein the NMDA receptor antagonist is ketamine or a pharmaceutically acceptable salt thereof and the antidepressant is amitriptyline or a pharmaceutically acceptable salt thereof.

39. (Previously Presented) The method of claim 24, wherein the emulsion further comprises a lipophilic intradermal penetration enhancer.

40. (Withdrawn) The method of claim 39, wherein the lipophilic Intradermal penetration enhancer is isopropyl myristate, glycerol monolaurate, glycerol monooleate, glycerol monolinoleate, isopropyl isostearate, isopropyl linoleate, isopropyl myristate/fatty acid monoglyceride combination, isopropyl myristate/ethanol/L-lactic acid combination, isopropyl palmitate, methyl acetate, methyl caprate, or methyl laurate.

41. (Withdrawn) A method of inducing local anesthesia in a mammal comprising topically administering to the skin of a mammal in need thereof an emulsion comprising: (a) a therapeutically effective amount of an antidepressant or a pharmaceutically acceptable salt thereof; (b) a therapeutically effective amount of an NMDA receptor antagonists or a pharmaceutically acceptable salt thereof; (c) a lipophilic component; (d) water; and (e) a surfactant, wherein the emulsion is an oil in water emulsion.

42. (Withdrawn) The method of claim 41, wherein the emulsion has a mean oil droplet size within the range of about 0.01 microns to about 100 microns.

43. (Withdrawn) The method of claim 41, wherein the emulsion has a mean oil droplet size within the range of about 0.1 microns to about 10 microns.

44. (Withdrawn) The method of claim 41, wherein the antidepressant is a norepinephrine reuptake inhibitor, a selective serotonin reuptake inhibitor, a monoamine oxidase inhibitor, a serotonin and noradrenaline reuptake inhibitor, a corticotropin releasing factor antagonist, an  $\alpha$ . adrenoreceptor antagonist, an NK1 receptor antagonist, a 5 HT.sub.1A receptor agonist, a 5 HT.sub.1A receptor antagonist, a 5 HT.sub.1A receptor partial agonist, an atypical antidepressant, or an other antidepressant or a pharmaceutically acceptable salt thereof.

45. (Withdrawn) The method of claim 44, wherein the antidepressant is a norepinephrin reuptake inhibitor or a pharmaceutically salt thereof.

46. (Withdrawn) The method of claim 41, wherein the antidepressant is a tricyclic depressant or a pharmaceutically acceptable salt thereof.

47. (Withdrawn) The method of claim 46, wherein the tricyclic antidepressant is amitriptyline, desmethyramitriptyline, clomipramine, doxepin, imipramine, imipramine N-oxide, trimipramine; adinazolam, amitriptylinoxide, amoxapine, desipramine, maprotiline, nortriptyline, protriptyline, amineptine, butriptyline, demexiptiline, dibenzepin, dimetacrine, dothiepin, fluacizine, iprindole, lofepramine, melitracen, metapramine, norclolipramine, noxiptilin, opipramol, perlapine, pizotyline, propizepine, quinupramine, reboxetine, or tianeptine or a pharmaceutically acceptable salt thereof.

48. (Withdrawn) The method of claim 41, wherein the antidepressant is amitriptyline or a pharmaceutically acceptable salt thereof.

49. (Withdrawn) The method of claim 41, wherein an amount of the antidepressant is within the range of about 0.1% by weight to about 10% by weight of a total weight of the emulsion.

50. (Withdrawn) The method of claim 41, wherein the NMDA receptor antagonist is one that binds to the NMDA receptor at the glycine binding site, the glutamate binding site, the PCP binding site, the polyamine binding site, or the zinc binding site or a pharmaceutically acceptable salt thereof.

51. (Withdrawn) The method of claim 50, wherein the NMDA receptor antagonist is one that binds to the NMDA receptor at the PCP binding site or a pharmaceutically acceptable salt thereof.

52. (Withdrawn) The method of claim 41, wherein the NMDA receptor antagonist is ketamine, phencyclidine, dextromethorphan, dextrophan, dexoxadrol, dizocilpine, remacemide, thienylcyclohexylpiperidine, N-allylnormetazocine, cyclazocine, etoxadrol, (1,2,3,4,9,9a hexahydro-fluoren-4a-yl)-methyl-amine, (1,3,4,9,10,10a-hexahydro-

2H-phenanthren-4a-yl)methyl-amine, PD 138558, tiletamine, kynurenic acid, 7-chloro-kynurenic acid, memantine, 6-cyano-7-nitroquinoxaline-2,3-dione, or 6,7-dinitroquinoxaline-2,3-dione or a pharmaceutically acceptable salt thereof.

53. (Withdrawn) The method of claim 41, wherein the NMDA receptor antagonist is ketamine or a pharmaceutically acceptable salt thereof.

54. (Withdrawn) The method of claim 41, wherein an amount of the NMDA receptor antagonist is within the range of about 0.1% by weight to about 10% by weight of a total weight of the emulsion.

55. (Withdrawn) The method of claim 41, wherein the NMDA receptor antagonist is ketamine or a pharmaceutically acceptable salt thereof and the antidepressant is amitriptyline or a pharmaceutically acceptable salt thereof.

56. (Withdrawn) The method of claim 41, wherein the emulsion further comprises a lipophilic intradermal penetration enhancer.

57. (Withdrawn) The method of claim 56, wherein the lipophilic intradermal penetration enhancer is isopropyl myristate, glycerol monolaurate, glycerol monooleate, glycerol monolinoleate, isopropyl isostearate, isopropyl linoleate, isopropyl myristate/fatty acid monoglyceride combination, isopropyl myristate/ethanol/L-lactic acid combination, isopropyl palmitate, methyl acetate, methyl caprate, or methyl laurate.

58. (Previously Presented) The method of claim 24, wherein the emulsion further comprises a humectant or an anti-foaming agent

59. (New) A method of treating pain in a mammal comprising topically administering to the skin of a mammal an emulsion comprising:

- (a) a therapeutically effective amount of an antidepressant or a pharmaceutically acceptable salt thereof;
- (b) a therapeutically effective amount of N-methyl-D-aspartate receptor antagonist or a pharmaceutically acceptable salt thereof;
- (c) a lipophilic component;



(d) water;

(e) a surfactant, wherein the emulsion is an oil in water emulsion, and

wherein the NMDA receptor antagonist is one that binds to the NMDA receptor at the glycine binding site, the glutamate binding site, the phencyclidine binding site, the polyamine binding site, or the zinc binding site, and

wherein the NMDA receptor antagonist is one that binds to the NMDA receptor at the PCP binding site.